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## **PROLONGED MOLECULAR REMISSIONS AFTER TANDEM AUTOLOGOUS-NONMYELOABLATIVE ALLOGRAFTING IN NEWLY DIAGNOSED MYELOMA**

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Allografting induces persistent molecular remissions (MR) in multiple myeloma (MM). We here present the results of minimal residual disease (MRD) analyses by nested qualitative PCR (Nested-PCR) and real time quantitative (RQ)-PCR in 26 patients (pts) with stage II-III MM treated with a tandem auto-allo approach. Transplants consisted of an autograft followed by non-myeloablative 200 cGy TBI and an allograft. BM samples were collected at diagnosis, after the autograft, at month 1, 3, 6 after the allograft and then every 6 months. Nested-PCR and RQ-PCR analyses were carried out using patient-specific primers as previously described (Voena, Leuk 1997; Ladetto, BBMT 2000). For outcome analysis pts were grouped according to reported criteria (Ladetto, ASH 2011): FullMR and StandardMR indicated MRD negativity on two consecutive samples by nested-PCR or by RQ-PCR respectively. Nineteen/26 pts had a molecular marker. At a median follow-up of 10,5 years (5,2-13,9) from diagnosis and 9,9 years (4,2-12,9) from the allograft, overall survival (OS) was 61% and median progression-free survival was 5,2 years. Transplant-related mortality occurred in 3/19 pts (16%), while 5/19 pts (26%) died of disease progression. Overall, cumulative incidence of non-relapse mortality (NRM) was 16%. MRD analysis showed that after the autograft 3/19 pts (16%) were negative by nested-PCR. After the allograft, the rate of PCR negativity remained low at month 1 (3/19, 16%) and 3 (5/19, 26%). However, PCR negativity went up to 44% (8/18) at 6 months and 47% (7/15) at one year post-transplant. Overall, 8 pts achieved FullMR at a median time from allograft of 6 months (1-12) and for a median duration of 33 months (6-102). Overall, 8 relapses occurred, 6 among 11 pts who never achieved FullMR and 2 in 8 pts who reached FullMR. Of these one has incomplete follow up and in the other one clinical relapse was heralded by a molecular relapse. Pts in FullMR had lower relapse incidence (27% vs 55%  $p=0,189$ ) and better median OS (not reached vs  $p=0,027$ ) than pts who did not achieve FullMR. StandardMR occurred in 12/19 pts (63%) during the first 24 months post-transplant, at a median time of 2 months (1-18) and for a median duration of 27 months (3-102). Pts in StandardMR showed lower relapse incidence (RI) (27% vs 71%  $p=0,016$ ) and better median OS (not reached vs  $p=0,05$ ) as compared to pts with positive PCR.